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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,986	09/07/2006	Ryuji Ueno	Q80545	9326

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EXAMINER	
THOMAS, TIMOTHY P	

ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
12/13/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/591,986	**Applicant(s)** UENO ET AL.	
	Examiner TIMOTHY P. THOMAS	**Art Unit** 1628	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 06 December 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-10*.
   Claim(s) withdrawn from consideration: *11-19*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Timothy P Thomas/
Examiner, Art Unit 1628

Continuation of 11. does NOT place the application in condition for allowance because: The rejection of record is maintained for the reasons of record:

Claims 1-10 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Inoue, et al. (WO 2004/067521 A1; priority date 2003 Jan 27; IDS 3/30/2007 reference) and Ogata et al. (US 4,780,465; 1988); in view of Niebergall ("Ionic Solutions and Electrolytic Equilibira); 2000; "Remington: The Science and Practice of Pharmacy"; 20th Ed.; Gennaro, Ed.; Lippincott Williams & Wilkins; Chapter 17, pp. 227-245).

Applicant argues Niebergall has been misapplied in the Office Action; that Niebergall provides general chemical knowledge about salting out, however, the NaCl concentration used therein is quite high and, therefore is not applicable as a reference in connection with providing an aqueous composition for pharmaceutical use such as for ocular topical administration. There is no limitation in the claims that recites any pharmaceutical use or topical ocular administration; claim 1 simply recites "a composition consisting essentially of a thiazole derivative of the formula (I)..."

Applicant argues that the problem to be solved by the instant invention is to stabilize and to improve solubility of the compound specified in the claim in an isotonic aqaueous composition; that the inventors have found for the first time that the compound recited in claim 1 *(thiazole compound having the guanidyl group) salts out in a solution having an osmotic ratio to saline of about 1 (0.85% NaCl solution); that the inventors have identified this problem for the first time; that Inoue is silent about the above discussed problem of the compound having a guanidyl group. Applicant further argues that the specification discusses the aqueous composition of the present invention is used as a pharmaceutical composition; that the composition to be administered topically to the eyes, and must be isotonic with the body fluid in the eye, and the osmotic ratio of the aqueous composition to saline (isotonic sodium chloride solution) must be around 1; that it is important whether or not the ingredient salts out when it is put in a solution having the osmotic ratio to saline or around 1; that 0.85% sodium chloride concentration gives the osmotic ratio to saline of 0.94; however, in contrast, 0.5M NaCl solution equals to 2.92% (w/v) NaCl solution, and the calculated osmotic ratio to saline will be 3.24; that human beings cannot accept such hypertonic solution as that disclosed in Niebergall as an opthalmic solution, injectable solution and the like; that the art knows that tere is no need to be concerned about salting out due to such a high concentration of NaCl for preparing pharmaceutical compositions; that, accordingly, Niebergall is not relevant prior art.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., that the claimed composition is a pharmaceutical composition intended to be administered topically to the eyes, which must be isotonc with the body fluid in the eye, and osmotic rations of the composition to saline levels must be around 1) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

MPEP 2144 (IV) indicates the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. Se In re Kahn, 441 F.3d 977, 987, 78 USPQ2d, 1329, 1336 (Fed. Cir 2006)...("One of ordinary skill in the art need not see the identical problem addressed in a prior art reference to be motivated to apply its teachings."). In the instant case, the fact that the same problem identified by applicant is not identified in the art is not critical to the rejection. The rejection establishes that general phenomena of salting out is known, and that the claimed additives are known in the art for the same purpose as NaCl, rendering the substitution of a claimed compound for NaCl as isotonic agents, giving the claimed composition.

The point of Niebergall is that salting out is a recognized phenomena in the art, providing an additional rationale to look to other compounds, i.e., glycerin, mannitol or boric acid, instead of the alternate NaCl, taught by Ogata as isotonic agents. The substitution of one art recogninzed isotonic agent for another is consistent with KSR rationale (B) simple substitution of one known element (glycerin, mannitol or boric acid) for another (NaCl) to obtain predictable results (isotonic solutions), see MPEP 2141 (III) and MPEP 2143. One of skill in the art would not limit Niebergall to solutions containing 0.5M NaCl as the only application of the recognized salting out phenomena, but a phenomena that should be considered for any formulation that might be using significant amounts of NaCl, such as isotonic solutions.

Applicant argues Ogata discloses aqueous compositions that contain quinolone carboxylic acid; that the compound disclosed in Ogata does not have guanidyl group; that since Inoue gives no suggestion about the problem to be solved by the instant invention, the art will not come up with the necessity of adjusting the osmotic pressure of the composition without using NaCl. This is not persuasive; the record indicates Ogata teaches NaCl, glycerin, mannitol, boric acid and glucose are isotonic agents for aqueous solutions (col.3, Table I). It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute any one of glycerin, mannitol, or boric acid for glucose in the aqueous parenteral solutions taught by Inoue as isotonic agents. The motivation would have been the art-recognized equivalence of the compounds for the purpose of adjusting isotonic strength of the aqueous solutions. Additionally the record indicates the salting out phenomena, taught by Niebergall, provides additional motivation to substitute an alternate isotonic compound, i.e., glycerin, mannitol or boric acid instead of the alternate NaCl taught by Ogata as isotonic agents. The recognition of the salting-out phenomenon provides motivation to exclude NaCl, and select an alternate non-salt isotonic agent, giving the compositions of the instant claims. This establishes that utilizing glycerin, mannitol or boric acid in the place of NaCl is obvious.